REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 42 to 54 and 93 to 117 are currently pending (claims 1 to 41 and 55 to 92 were canceled, without prejudice, in Applicants' last response).

Claims added in the instant amendment

In the present response, claims 118 and 119 are added. Accordingly, after the entry of the instant amendment, claims 42 to 54 and 93 to 119 will be pending and under examination.

Restriction Requirement and Election

In the restriction requirement October 2, 2003, the Patent Office alleged that the pending claims of the application were directed to nine separate and distinct inventions under 35 U.S.C. §121. In Applicants' response to the Restriction Requirement, Group IV, claims 42 to 55, drawn to methods of generating a variant, was elected.

Outstanding Rejections

Claims 43 to 54, 93 and 108 to 117, are rejected under 35 USC §112, second paragraph. Claims 42 to 54, 93 and 95 to 117 are rejected under 35 USC §112, first paragraph. The rejection of claims 42, 43 and 50 under 35 USC §102(b) has been maintained, and claims 93, 95, 96 and 108 to 112 have been newly rejected, as allegedly anticipated by Trakulnaleamsai, et al., (1995) Ann. N.Y. Acad. Sci. 750:158-165 (hereinafter "Trakulnaleamsai"), as evidenced by Loprasert et al. (1989) J. Bacter. 171(9):4871-4875 (hereinafter "Loprasert"). The rejection of claims 42 to 53 under 35 USC §103(a) has been maintained, and claims 93, 95, 96 and 108 to 112 have been newly rejected, as allegedly unpatentable over Trakulnaleamsai in view of Short, U.S. Patent No. 5,939,250 (hereinafter "the Short '250 patent"). The rejection of claims 42, 43,

54 and 55 under 35 USC §103(a) as allegedly unpatentable over Trakulnaleamsai in view of Short, U.S. Patent No. 6,479,258 (hereinafter "the Short '258 patent") has been maintained. Claims 42 to 53 and 93 to 117 are newly rejected as allegedly unpatentable over Trakulnaleamsai in view of the Short '250 patent and Robertson, et al., WO 98/00526, published January 8, 1998.

Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Support for Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for claims wherein the modifications are introduced by synthetic gene reassembly can be found, inter alia, on page 13, lines 14 to 30. For example, support for claims wherein nucleic acids used in the methods of the invention can have a length of about 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of polynucleotide of the invention can be found, inter alia, on page 34, lines 21 to 31. Applicants submit that no new matter is introduced by the present amendments.

Information Disclosure Statement

Applicants thank the Examiner for considering and initialing the Information Disclosure Statement (IDS) submitted August 06, 2003. However, an initialed copy of the IDS submitted June 23, 2003, was not included with the instant office action. For the Examiner's convenience, a copy of the June 23, 2003, IDS is enclosed herein. It is respectfully requested that the cited information be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Issues under 35 U.S.C. §112, second paragraph

The Patent Office rejected claims 42 to 54, 93, and 108 to 117, under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants' regard and the invention. In particular, the Patent Office had concerns regarding claims 93 and 108 to 117. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

Written Description

Claims 42 to 54, 93 and 95 to 117 are rejected under 35 USC §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

The Patent Office alleges, inter alia, that the specification does not contain any disclosure of the function of all nucleic acid variants of either SEQ ID NO:5 or SEQ ID NO:7 used in the claimed methods (please note, e.g., page 3, lines 12 to 15, of the office action). To address this issue, claims directed to use of a genus of nucleic acids (including a genus defined by a percent sequence identity or stringent hybridization to an exemplary nucleic acid) have been amended to be directed to methods for generating variants comprising providing a genus of catalase-encoding nucleic acids. Please note that the specification describes an exemplary assay to screen for catalase activity (and thus determine whether a nucleic acid is within the scope of the claimed methods) in, inter alia, Example 2, pages 72 to 73 of the specification.

It is further alleged that disclosing two species of nucleic acids to be used in the claimed methods is insufficient to put one of skill in the art in possession of the attributes and features of all species with the genus used in the claimed methods (please note, e.g., the last line of page 3 of the office action).

Applicants respectfully submit that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., a % sequence identity or stringent hybridization to an exemplary nucleic acid, e.g., SEQ ID NO:5 or SEQ ID NO:7) and function (e.g., encoding a polypeptide having catalase activity) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully aver that the two disclosed catalase-encoding nucleic acid species of the invention is sufficient to put one of skill in the art in possession of the attributes

and features of all species within the genus used in the claimed methods. In fact, both the Patent Office and the Federal Circuit set forth conditions where a single species is sufficient to put one of skill in the art in possession of the attributes and features of all species within a genus, where the genus is defined in terms of shared physical and structural properties with the single species.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph, and note that the guidelines state that a description of a genus of polynucleotides in terms of its physico-chemical properties, e.g., a % sequence identity, to a single exemplary species, and a common function satisfies the written description requirement of section 112, first paragraph, for the genus of polynucleotides.

In Example 14 of the Guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of Example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids used in the methods of the invention is described by structure (the exemplary SEQ ID NO:5 or SEQ ID NO:7), a physico-chemical property (a percent sequence identity or stringent hybridization to SEQ ID NO:5 or SEQ ID NO:7) and function (having catalase activity). All species of the genus used in the claimed methods (after entry of the instant amendment) must have at least 65% or more sequence identity to a sequence as set forth in SEQ ID NO:5 or SEQ ID NO:7. The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-

chemical property (e.g., a % sequence identity) and a defined function, the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth, inter alia, in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the catalase-encoding nucleic acids used in the claimed methods. In one aspect, the genus of nucleic acids used in the claimed methods all must have catalase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary nucleic acid. Therefore, the genus of catalases used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

> Similarly, in this court's most recent pronouncement, it noted:
>
> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.
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> Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the catalase-encoding nucleic acids used in the claimed methods is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or stringent

hybridization). Accordingly, the sequences of the invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that claimed invention is sufficiently described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 42 to 54, 93 and 95 to 117, are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for methods of generating a variant catalase comprising creating a library of variants to SEQ ID NO:5 or SEQ ID NO:7, expressing the modified sequences, screening the proteins produced from the modified sequences for catalase activity and selecting a variant sequence which encodes a protein having catalase activity.

However, the Patent Office alleges that the specification does not reasonably provide enablement for the extremely large number of methods (the large number of nucleic acids used in the methods) broadly encompassed by the claims. It is alleged, inter alia, that predictability of which changes can be tolerated in a protein's amino acid sequence and obtain a desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification.

To address the Patent Office's concerns, Applicants submit for consideration a Rule 132 expert declaration by Dr. Jay Short, who was an expert in the field of molecular biology and enzyme development at the time of the invention. Dr. Short declares that procedures for modifying nucleic acids were conventional and routine in the art at the time of the invention. Dr. Short declares that one of ordinary skill in the art using the teaching of the specification would have been able to make a catalase-encoding nucleic acid having at least 65% sequence

identity to SEQ ID NO:5 or SEQ ID NO:7, or a catalase-encoding nucleic acid comprising at least 30 or 35 or more consecutive nucleotides of a sequence having at least 65% sequence identity to SEQ ID NO:5 or SEQ ID NO:7, or a catalase-encoding nucleic acid that hybridizes under the defined stringent hybridization conditions, to practice the methods of the invention without undue experimentation. Dr. Short declares that it was considered routine by one skilled in the art at the time of the invention to screen for multiple substitutions or multiple modifications in a nucleic acid sequence for functional variations, including screening for a genus of catalase-encoding nucleic acids. For example, high through-put methods for screening for enzyme activity, such as catalase activity, were well known in the art. Dr. Short declares that while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (e.g., finding a genus of nucleic acids encoding catalases) predictable. Accordingly, Dr. Short declares that at the time of the invention it would have been considered routine by one skilled in the art to generate and screen multiple substitutions or multiple modifications in an exemplary nucleic acid sequence and predictably generate a genus of nucleic acids encoding catalases.

Dr. Short declares that it was not necessary for the skilled artisan to understand which specific regions of catalase structure may be modified without affecting function or activity, or, which specific regions of catalase structure should be modified to generate altered enzyme activity, to practice the methods of the invention because methods for modifying sequences, generating catalase-encoding sequences and screening for activity at the time of the invention were routine and predictable. For example, Dr. Short declares that methods for sequence modifications were sufficiently routine and predictable at the time of the invention to predictably generate catalase-encoding sequences without need of knowing which specific regions of catalase structure affect catalase function or activity. For example, on pages 30 to 33, the specification gives a detailed description of an exemplary method for sequence modification called Gene Site Saturation Mutagenesis™ (GSSM™). Dr. Short declares that in one aspect of GSSM™, degenerate oligonucleotides comprising degenerate N,N,N cassettes can be used for subjecting each original codon in a parental polynucleotide template to a full range of codon substitutions. Thus, GSSM™ allows for mutagenizing each and every amino acid position in a parental polypeptide to generate amino acid changes that can be routinely screened for their

effect on activity. Dr. Short declares that another exemplary method for sequence modification, called synthetic gene reassembly, or SLR, is described on pages 13 to 15 of the specification. As noted in the specification on page 15, lines 15 to 24, SLR allows a systematic examination and screening procedure to be performed, allowing a potentially very large number of progeny molecules to be examined systematically in smaller groups. Dr. Short declares that methods known at the time of the invention for modifying nucleic acid sequences, such as GSSM™, SLR, or the other methods described in the specification, in combination with high through-put enzyme activity screening known at the time of the invention, made methods that require previous knowledge of protein tertiary structure, active sites and the like obsolete and unnecessary. Accordingly, Dr. Short declares that using methods known in the art at the time of the invention, e.g., GSSM™ or SLR, it would not have been necessary to understand which specific regions of catalase structure needed to be modified to generate the genus of nucleic acids for practicing the methods of the invention.

Dr. Short declares that the specification provides sufficient guidance to one of ordinary skill in the art as to whether a nucleic acid falls within the scope of the genus used in the claimed methods. Dr. Short declares that methods for determining the requisite structure (sequence based on percent sequence identity to an exemplary nucleic acid) and function (catalase activity) are clearly set forth in the specification. Dr. Short declares that at the time of the invention, high through-put *in vivo* (e.g., whole cell) nucleic acid expression and enzyme activity screening protocols were well known in the art. The specification sets forth an exemplary catalase screening assay to determine if a nucleic acid is within the scope of the genus used in the claimed methods, inter alia, on pages 72 to 73, Example 2. Dr. Short declares that methods for determining sequence identity were also routine and well known in the art at the time of the invention. The specification describes methods for determining whether a nucleic acid has a percent sequence identity to an exemplary polynucleotide on, inter alia, pages 55 to 70 of the specification. As declared by Dr. Short, all of these protocols were routine in the art at the time of the invention and positive results (e.g., determining if a nucleic acid is within the scope of the genus used in the claimed methods, e.g., a catalase-encoding nucleic acid at least 30 consecutive nucleotides of a sequence having at least 65% identity to SEQ ID NO:5 or SEQ ID NO:7) predictable. Dr. Short declares that while the numbers of alternative species that needed

to be screened may have been high, the protocols for screening were routine and positive results predictable. Accordingly, the specification provided sufficient guidance to one of ordinary skill in the art to make and use the described genus of nucleic acid to practice the claimed methods.

Whether large numbers of compositions (e.g., nucleic acids, enzymes, antibodies, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognized the need to screen numbers of negatives to find a sample that has the desired properties, e.g., catalase-encoding activity. Furthermore, as declared by Dr. Short, methods of making and screening procedures used to identify nucleic acids used in the claimed methods (e.g., identifying the genus of catalase-encoding nucleic acids) were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the

skilled artisan using Applicants' written disclosure could have practiced the instant claimed invention without undue experimentation.

Applicants respectfully submit that the pending claims meet the enablement requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that the specification sufficiently described how to make and use the claimed methods to satisfy the requirements of 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Trakulnaleamsai and Loprasert

The rejection of claims 42, 43 and 50 under 35 USC §102(b) has been maintained, and claims 93, 95, 96 and 108 to 112 have been newly rejected, as allegedly anticipated by Trakulnaleamsai, as evidenced by Loprasert.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

The Patent Office alleges that a nucleic acid taught by Trakulnaleamsai is 61% identical to SEQ ID NO:7. It is also alleged that a nucleic acid taught by Trakulnaleamsai has at least two regions of 33 nucleotides each having 91% sequence identity to SEQ ID NO:5.

The claims have been amended to address these issues. After entry of the instant amendment, the claimed invention is directed to, inter alia, methods of generating a polynucleotide comprising obtaining a nucleic acid comprising a sequence having at least about 65% sequence identity to a sequence as set forth in SEQ ID NO:7 or SEQ ID NO:5, wherein the sequence encodes a polypeptide having catalase activity, and, methods of generating a polynucleotide comprising obtaining a nucleic acid comprising at least about 35 consecutive nucleotides of a sequence having at least about 65% sequence identity to SEQ ID NO:5 or at least about 30 consecutive nucleotides of a sequence having at least about 65% sequence identity to SEQ ID NO:7, wherein the sequence encodes a polypeptide having catalase activity. Accordingly, Trakulnaleamsai is not a single prior source that contains each and every limitation of the claimed invention.

Applicants also note that Loprasert does not teach a nucleic acid of the invention and Loprasert does not teach a method using a nucleic acid of the invention.

Applicants respectfully aver that, after entry of the instant amendment, Trakulnaleamsai, as evidenced by Loprasert, is not a single prior source that contains each and every limitation of the claimed invention. Accordingly, the rejection of the claims under 35 U.S.C. §102(b) as allegedly anticipated by Trakulnaleamsai, as evidenced by Loprasert, can be withdrawn.

Issues under 35 U.S.C. §103

Trakulnaleamsai in view of the Short '250 patent

The rejection of claims 42 to 53 under 35 USC §103(a) has been maintained, and claims 93, 95, 96 and 108 to 112 have been newly rejected, as allegedly unpatentable over Trakulnaleamsai in view of the Short '250 patent.

As discussed above, after entry of the instant amendment, Trakulnaleamsai is not a single prior source that contains each and every limitation of the claimed invention. After entry of the instant amendment, Trakulnaleamsai will be defective in that it will not teach any nucleic acid used in the methods of the invention. Because the Short '250 patent does not teach or suggest a nucleic acid of the invention, it cannot cure the defect in Trakulnaleamsai. Accordingly, Trakulnaleamsai in view of the Short '250 patent does not teach or suggest the claimed invention.

Trakulnaleamsai in view of the Short '258 patent

The rejection of claims 42, 43, 54 and 55 under 35 USC §103(a) as allegedly unpatentable over Trakulnaleamsai in view of the Short '258 patent has been maintained.

As discussed above, after entry of the instant amendment, Trakulnaleamsai is not a single prior source that contains each and every limitation of the claimed invention. After entry of the instant amendment, Trakulnaleamsai will be defective in that it will not teach any nucleic acid used in the methods of the invention. Because the Short '258 patent does not teach or suggest a nucleic acid of the invention, it cannot cure the defect in Trakulnaleamsai. Accordingly, Trakulnaleamsai in view of the Short '258 patent does not teach or suggest the claimed invention.

Trakulnaleamsai in view of the Short '250 patent and Robertson

Claims 42 to 53 and 93 to 117 are newly rejected as allegedly unpatentable over Trakulnaleamsai in view of the Short '250 patent and Robertson, et al., WO 98/00526, published January 8, 1998.

As discussed above, after entry of the instant amendment, Trakulnaleamsai is not a single prior source that contains each and every limitation of the claimed invention. After entry of the instant amendment, Trakulnaleamsai will be defective in that it will not teach any nucleic acid used in the methods of the invention. As discussed above, the Short '250 patent does not teach or suggest a nucleic acid of the invention. Accordingly, Trakulnaleamsai in view of the Short '250 patent does not teach or suggest the claimed invention.

Regarding Robertson, et al., WO 98/00526, the Patent Office alleges that because the disclosure of the parent application USSN 08/674,887, filed July 3, 1996, fails to disclose methods of mutagenesis, the claimed invention cannot claim priority to this parent application. However, Applicants respectfully aver that the parent disclosure USSN 08/674,887, filed July 3, 1996, sufficiently describes the instant claimed invention to satisfy the requirements of section 112, first paragraph, and the instant claimed methods can properly claim priority back to USSN 08/674,887, filed July 3, 1996.

For example, claim 42 and claim 93 are drawn to methods of generating a variant nucleic acid comprising obtaining a nucleic acid of the invention and modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence. Support for pending claims 42 and 93 is clearly found in the parent specification, inter alia, on page 8, third paragraph (see also the paragraph spanning pages 8 to 9 of WO 98/00526):

> The present invention relates to polynucleotides which differ from the reference polynucleotide such that the differences are silent, for example, the amino acid sequence encoded by the polynucleotides is the same. The present invention also relates to nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference polynucleotide. In a preferred aspect of the invention these polypeptides retain the same biological action as the polypeptide encoded by the reference polynucleotide.

Support for pending claims 42 and 93 can also be found in the parent specification, inter alia, on page 9, fourth full paragraph:

> Thus, the present invention includes polynucleotides encoding the same mature enzymes as shown in FIGS. 1-2 (SEQ ID NOS: 6 & 8) as well as variants of such polynucleotides which variants encode for a fragment, derivative or analog of the enzymes of FIGS. 1-2 (SEQ ID NOS: 6 & 8). Such nucleotide variants include deletion variants, substitution variants and addition or insertion variants.

Accordingly, the parent disclosure USSN 08/674,887, filed July 3, 1996, sufficiently describes the instant claimed invention to satisfy the requirements of section 112, first paragraph, and the instant claimed methods can properly claim priority back to USSN 08/674,887, filed July 3, 1996. Thus, Robertson, et al., WO 98/00526, published after the priority date of the instant application, is not prior art to the instant application.

Applicants also note that Robertson, et al., WO 98/00526, is the publication of PCT/US97/16513, which has a common priority document to the instant application: USSN 08/674,887, filed July 3, 1996. The instant application is a CIP of USSN 08/951,844, which is a divisional of USSN 08/674,887. Applicants submit that the claimed invention can properly claim priority for the sequences of the invention back to USSN 08/674,887, filed July 3, 1996.

Accordingly, Applicants respectfully aver that the rejection of the claims under 35 U.S.C. §103(a) can be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102(b) and 35 U.S.C. §103(a). Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

Date: April 22, 2004

Gregory P. Einhorn
Reg. No. 38,440

Morrison & Foerster LLP
3811 Valley Centre Drive, Suite 500
San Diego CA 92130
direct dial 858 720 5133
fax 858 720 5125